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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/586,141

07/02/2007

Mara Rossi

ROSSI 10

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EXAMINER

SEHARASEYON, JEGATHEESAN

ART UNIT

PAPER NUMBER

1646

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/586,141	<b>Applicant(s)</b> ROSSI ET AL.	
	<b>Examiner</b> JEGATHEESAN SEHARASEYON	<b>Art Unit</b> 1646	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 8/31/09.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 July 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>7/17/06</u> . | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. This Office Action is in response to Applicant's response filed 8/31/09. Claims 1-5 are pending and examined.

#### ***Information Disclosure Statement***

2. The IDS filed 7/17/06 has been considered

#### ***Claim Objections***

3. E.coli in claim 3 has to be written in "italics".

#### ***Claim Rejections - 35 USC § 112 (Second paragraph)***

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4a. Claim 1 is an improper Jepson claim. For example: A phrase such as "wherein the improvement comprises," and those elements, steps, and/or relationships which constitute that portion of the claimed combination which the applicant considers as the new or improved portion (see 37 CFR 1.75(e)). Claims 2-5 are rejected in so far as they are dependent on claim 1.

4b. Claim 1 recites the limitation "the step of solubilization" in lines 3-4. There is insufficient antecedent basis for this limitation in the claim.

#### ***Claim Rejections - 35 USC § 112 (first paragraph)***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5a. Claim 5 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim recites a genus of chemokine polypeptides that are mutant of SEQ ID NO: 1. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a recitation that chemokine is a mutant of SEQ ID NO: 1. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

*Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991), clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.)

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The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116).

With the exception of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir.1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483 (BPAI 1993). In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only process comprising the amino acid sequence set forth in SEQ ID NO: 1, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

5b. Claim 5 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed process wherein the recited

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chemokine polypeptide of SEQ ID NO: 1, does not reasonably provide enablement for the claimed process using chemokine polypeptide mutant of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims, as recited read on chemokine mutant of SEQ ID NO: 1. The specification indicates that human RANTES triple mutant is contemplated (pg 10, lines 10-15). It is not clear which amino acids are changed to become triple mutant. There is no extensive information on artificially mutated forms of this protein. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, *Biochemistry* 29:8509-8517; Ngo et al., 1994, *The Protein Folding Problem and Tertiary Structure Prediction*, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to

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determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity.

Due to the large quantity of experimentation necessary to determine which mutant chemokine of SEQ ID NO: 1 would be functional, the lack of direction/guidance presented in the specification regarding such variants, the absence of any working examples, the complex nature of the invention, the state of the prior art establishing the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite meaningful structural and functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6a. Claims 1- 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Musacchio et al. (1996) provided in the IDS of 7/17/06.

Musacchio et al. disclose a process for the recovery of Opc protein expression E.coli as inclusion bodies wherein the recombinant protein is solubilized and purified on a reversed phase chromatography (RP-HPLC). The eluted protein is finally refolded (abstract, pg. 752). Therefore, claims 1-3 are anticipated by Musacchio et al. (1996).

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7a. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Musacchio et al. (1996) in view of Li et al. (WO98/14467) and Proudfoot et al. (WO02/28419) both provided in the IDS of 7/17/06.

The teachings of Musacchio et al. have been disclosed above in paragraph 6a. However, the reference does not teach the purification of chemokine protein using RP-HPLC.

Li et al. teach a method of purifying chemokine from inclusion bodies wherein a reverse phase chromatography step is added to purify the protein after the renaturation step (pg 24, ln. 20- pg. 29, lin15). The reference also discloses mutant chemokines (pg. 61). Although, RP-HPLC is used it is not interposed between solubilization and renaturation. Proudfoot et al. disclose a triple mutant of RANTES (a chemokine) polypeptide that is expressed in E.coli and purified. As shown below it is a mutant of

SEQ ID NO: 1

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AAO21081

ID AAO21081 standard; protein; 91 AA.

XX

AC AAO21081;

XX

DT 19-JUL-2002 (first entry)

XX

DE Protein of triple 40's RANTES (3-68) mutant.

XX

KW RANTES; neuroprotective; antiallergic; antiinflammatory; anti-HIV; human;

KW chemokine mutant; cationic site; multiple sclerosis; HIV infection;

KW inflammatory disease; demyelinating disease; allergic; mutein.

XX

OS Homo sapiens.

OS Synthetic.

XX

PN WO200228419-A2.

XX

PD 11-APR-2002.

XX

PF 03-OCT-2001; 2001WO-EP011428.

XX

PR 04-OCT-2000; 2000EP-00121665.

XX

PA (ISTF ) ARS APPLIED RES SYSTEMS HOLDING NV.

XX

PI Proudfoot A, Wells TNC, Kosco-Vilbois M;

XX

DR WPI; 2002-340073/37.

XX

PT A mutant of the human CC chemokine RANTES with two mutations in the  
PT cationic site of the 40's loop is used for treatment of multiple  
PT sclerosis and/or demyelinating diseases.

XX

PS Claim 1; Page 37; 46pp; English.

XX

CC The invention relates to a truncated and mutated human RANTES (a CC  
CC chemokine mutant), comprising the amino sequence of 91 amino acids as  
CC given in the specification. The CC chemokine mutant RANTES, with two  
CC mutations in the cationic site is useful for the preparation of a  
CC pharmaceutical composition used in treating multiple sclerosis or other  
CC demyelinating diseases. The mutant with single mutations at cationic  
CC sites is used for the treatment of HIV infection and/or other allergic  
or  
CC inflammatory diseases. This sequence represents a mutant human RANTES  
CC protein of the invention

XX

SQ Sequence 91 AA;

Query Match 97.1%; Score 356.5; DB 1; Length 91;

Best Local Similarity 98.5%;

Matches 67; Conservative 0; Mismatches 0; Indels 1; Gaps

1;

```
Qy          1 SPYSSDTPCCFAYIARPLPRAHIKEYFYTSGKCSNPAVVFVTAANAQVC-NPEKKWVRE 59
              |||
Db          24 SPYSSDTPCCFAYIARPLPRAHIKEYFYTSGKCSNPAVVFVTAANAQVCANPEKKWVRE 83
              |||
Qy          60 YINSLEMS 67
              |||
Db          84 YINSLEMS 91
```

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the process of Musacchio et al. to purify chemokine mutant of SEQ ID NO: 1 by the teachings of Li et al. and Proudfoot et al. with a reasonable expectation of success because Li et al discloses the purification of chemokines from E. coli and Proudfoot discloses a mutant of SEQ ID NO: that is expressed in E. coli. The motivation to do so is provided by Proudfoot et al in its disclosure of the process of chemokine mutant purification. Therefore, 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Musacchio et al. (1996) in view of Li et al. (WO98/14467) and Proudfoot et al. (WO02/28419).

### ***Conclusion***

8. No claims are allowable.

### ***Contact Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JEGATHEESAN SEHARASEYON whose telephone number is (571)272-0892. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph. D can be reached on 571-272-0835. The fax phone

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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jegatheesan Seharaseyon,  
Examiner, Art Unit 1646

JS  
3/25/10